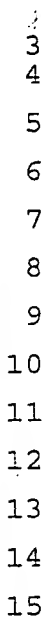


Sub A'

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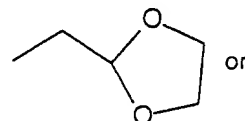


[REDACTED]

- $$\frac{1}{2}$$



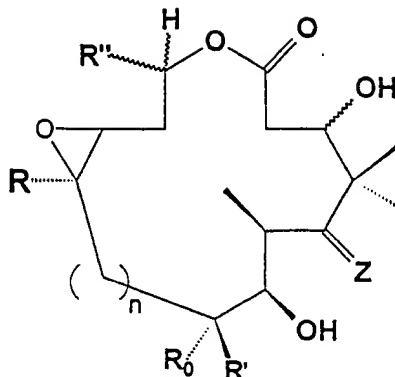
wherein R is H, methyl, ethyl, n-propyl, n-butyl, n-hexyl,



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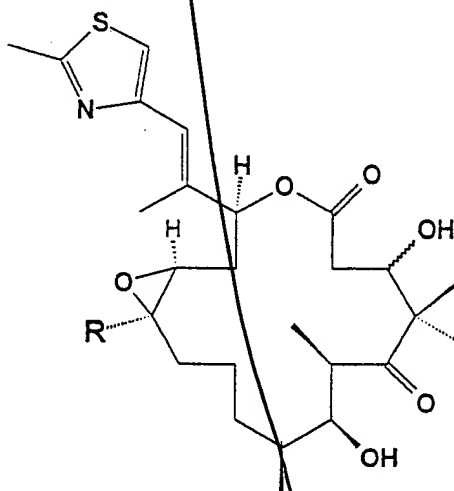
A compound having the structure:



wherein R, R₀, and R' are independently H, linear or branched chain alkyl, optionally substituted by hydroxy, alkoxy, carboxy, carboxaldehyde linear or branched alkyl or cyclic acetal, fluorine, NR₁R₂, N-hydroximino, or N-alkoxyimino, wherein R₁ and R₂ are independently H, phenyl, benzyl, linear or branched chain alkyl; wherein R" is -CHY=CHX, or H, linear or branched chain alkyl, phenyl, 2-methyl-1,3-thiazolynyl, 2-furanyl, 3-furanyl, 4-furanyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, imidazolyl, 2-methyl-1,3-oxazolynyl, 3-indolyl or 6-indolyl; and wherein X is H, linear or branched chain alkyl, phenyl, 2-methyl-1,3-thiazolynyl, 2-furanyl, 3-furanyl, 4-furanyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, imidazolyl, 2-methyl-1,3-oxazolynyl, 3-indolyl or 6-indolyl; wherein Y is H or linear or branched chain alkyl; wherein Z is O, N(OR₃) or N-NR₄R₅, wherein R₃, R₄ and R₅ are independently H or a linear or branched chain alkyl; and wherein n is 0, 1, 2, or 3.

4.

The compound of claim 3 having the structure:



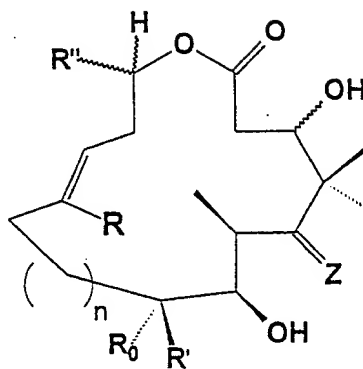
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wherein R is H, methyl, ethyl, n-propyl, n-butyl or n-hexyl.

1 5. A compound having the structure:

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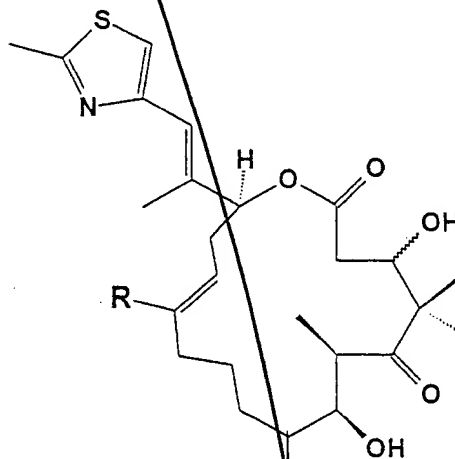


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4 wherein R, R₀, and R' are independently H, linear or branched chain alkyl, optionally
 5 substituted by hydroxy, alkoxy, carboxy, carboxaldehyde linear or branched alkyl or
 6 cyclic acetal, fluorine, NR₁R₂, N-hydroximino, or N-alkoxyimino, wherein R₁ and R₂
 7 are independently H, phenyl, benzyl, linear or branched chain alkyl; wherein R'' is -
 8 CHY=CHX, or H, linear or branched chain alkyl, phenyl, 2-methyl-1,3-thiazolynyl, 2-
 9 furanyl, 3-furanyl, 4-furanyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, imidazolyl, 2-methyl-1,3-
 10 oxazolynyl, 3-indolyl or 6-indolyl; and wherein X is H, linear or branched chain alkyl,
 11 phenyl, 2-methyl-1,3-thiazolynyl, 2-furanyl, 3-furanyl, 4-furanyl, 2-pyridyl, 3-pyridyl,
 12 4-pyridyl, imidazolyl, 2-methyl-1,3-oxazolynyl, 3-indolyl or 6-indolyl; wherein Y is H
 13 or linear or branched chain alkyl; wherein Z is O, N(OR₃) or N-NR₄R₅, wherein R₃, R₄
 14 and R₅ are independently H or a linear or branched chain alkyl; and wherein n is 0,
 15 1, 2, or 3.

1 6. The compound of claim 5 having the structure:

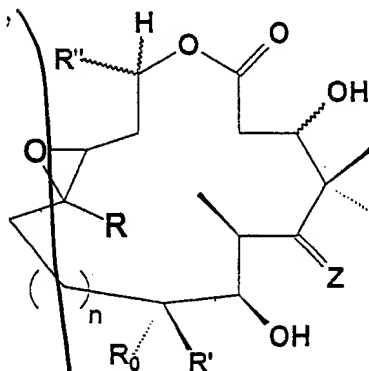
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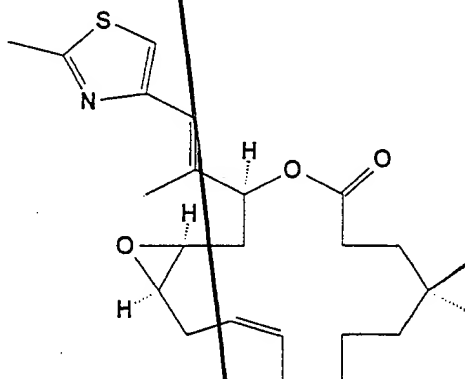
4 wherein R is H, methyl, ethyl, n-propyl, n-butyl, n-hexyl or hydroxypropyl.

1 7. A compound having the structure:

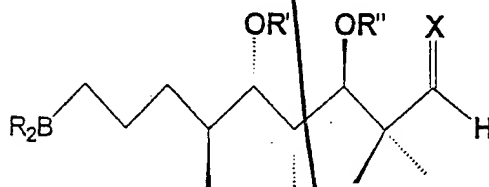


wherein R, R₀, and R' are independently H, linear or branched chain alkyl, optionally substituted by hydroxy, alkoxy, carboxy, carboxaldehyde linear or branched alkyl or cyclic acetal, fluorine, NR₁R₂, N-hydroximino, or N-alkoxyimino, wherein R₁ and R₂ are independently H, phenyl, benzyl, linear or branched chain alkyl; wherein R'' is -CHY=CHX, or H, linear or branched chain alkyl, phenyl, 2-methyl-1,3-thiazolynyl, 2-furanyl, 3-furanyl, 4-furanyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, imidazolyl, 2-methyl-1,3-oxazolynyl, 3-indolyl or 6-indolyl; and wherein X is H, linear or branched chain alkyl, phenyl, 2-methyl-1,3-thiazolynyl, 2-furanyl, 3-furanyl, 4-furanyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, imidazolyl, 2-methyl-1,3-oxazolynyl, 3-indolyl or 6-indolyl; wherein Y is H or linear or branched chain alkyl; wherein Z is O, N(OR₃) or N-NR₄R₅, wherein R₃, R₄ and R₅ are independently H or a linear or branched chain alkyl or alkoxy; and wherein n is 0, 1, 2, or 3.

8. A compound having the structure:



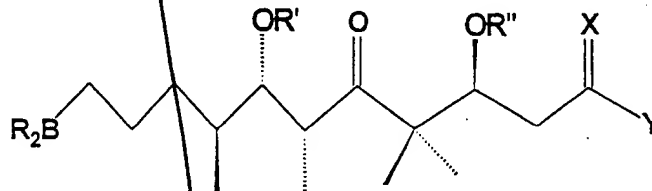
9. A compound having the structure:



wherein R' and R'' are independently hydrogen, a linear or branched alkyl,

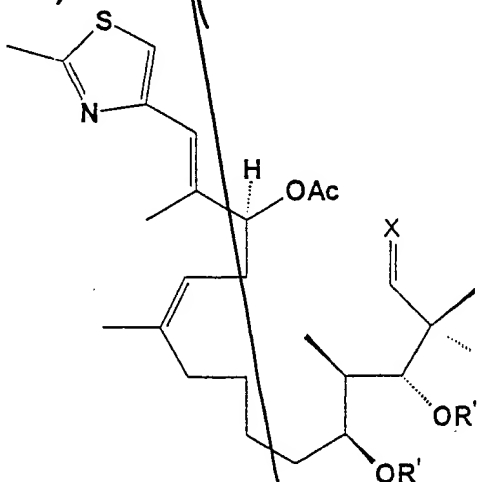
5 substituted or unsubstituted aryl or benzyl, trialkylsilyl, dialkylarylsilyl,
6 alkyldiarylsilyl, a linear or branched acyl, substituted or unsubstituted aroyl or
7 benzoyl; wherein X is oxygen, $(OR^*)_2$, $(SR^*)_2$, $-(O-(CH_2)_n-O)-$, $-(O-(CH_2)_n-S)-$ or $-(S-$
8 $(CH_2)_n-S)-$; wherein R^* is a linear or branched alkyl, substituted or unsubstituted aryl
9 or benzyl; wherein R_2B is a linear, branched or cyclic alkyl or substituted or
10 unsubstituted aryl or benzyl boranyl moiety; and wherein n is 2, 3 or 4.

1 10. A compound having the structure:
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3 wherein R' and R'' are independently hydrogen, a linear or branched alkyl,
4 substituted or unsubstituted aryl or benzyl, trialkylsilyl, dialkylarylsilyl,
5 alkyldiarylsilyl, a linear or branched acyl, substituted or unsubstituted aroyl or
6 benzoyl; wherein X is oxygen, $(OR^*)_2$, $(SR^*)_2$, $-(O-(CH_2)_n-O)-$, $-(O-(CH_2)_n-S)-$ or $-(S-$
7 $(CH_2)_n-S)-$; wherein R^* is a linear or branched alkyl, substituted or unsubstituted aryl
8 or benzyl; wherein R_2B is a linear, branched or cyclic alkyl or substituted or
9 unsubstituted aryl or benzyl boranyl moiety; wherein Y is OH, linear or branched
10 chain alkoxy, trimethylsilyloxy, t-butyl dimethylsilyloxy or methyl diphenylsilyloxy; and
11 wherein n is 2, 3 or 4.
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1 11. A compound having the structure:
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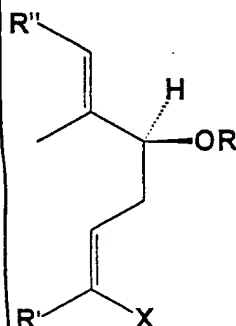
3 wherein R' and R'' are independently hydrogen, a linear or branched alkyl,
4 substituted or unsubstituted aryl or benzyl, trialkylsilyl, dialkylarylsilyl,
5 alkyldiarylsilyl, a linear or branched acyl, substituted or unsubstituted aroyl or
6 benzoyl; wherein X is oxygen, $(OR)_2$, $(SR)_2$, $-(O-(CH_2)_n-O)-$, $-(O-(CH_2)_n-S)-$ or $-(S-$
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8 ()-S) wherein n is 2, 3 or 4.

1 12. The compound of claim 11 wherein R' is TBS, R'' is TPS and X is (OMe)₂.

1 13. A compound having the structure:

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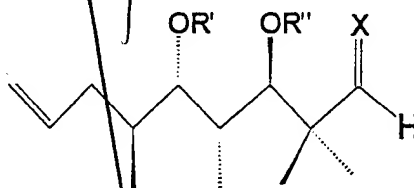
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4 wherein R is hydrogen, a linear or branched alkyl, alkoxyalkyl, substituted or
 5 unsubstituted aryloxyalkyl, linear or branched acyl, substituted or unsubstituted aroyl
 6 or benzoyl; wherein X is a halogen; wherein R'' is H, linear or branched chain alkyl,
 7 phenyl, 2-methyl-1,3-thiazolyl, 2-furanyl, 3-furanyl, 4-furanyl, 2-pyridyl, 3-pyridyl,
 8 4-pyridyl, imidazolyl, 2-methyl-1,3-oxazolyl, 3-indolyl or 6-indolyl; and wherein Y
 9 is H or linear or branched chain alkyl; wherein R' is H, linear or branched chain
 10 alkyl, hydroxymethyl, hydroxypropyl, alkyl carboxaldehyde, alkyl carboxaldehyde
 11 linear or cyclic acetal; and X is a halide.

1 14. The compound of claim 13 wherein R is acetyl and X is iodo.

1 15. A compound having the structure:

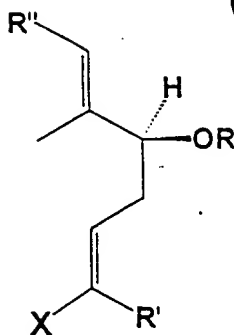
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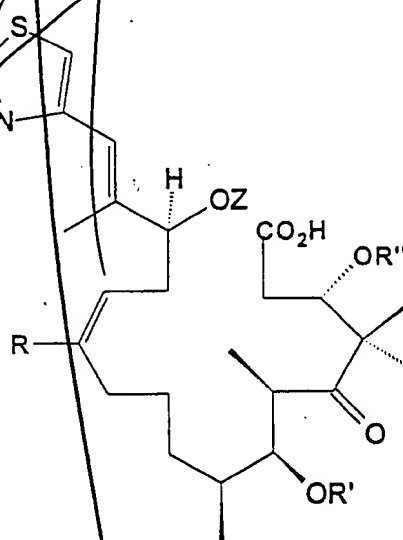
4 wherein R' and R'' are independently hydrogen, a linear or branched alkyl,
 5 substituted or unsubstituted aryl or benzyl, trialkylsilyl, dialkylarylsilyl,
 6 alkylarylsilyl, a linear or branched acyl, substituted or unsubstituted aroyl or
 7 benzoyl; wherein X is oxygen, (OR)₂, (SR)₂, -(O-(CH₂)_n-O)-, -(O-(CH₂)_n-S)- or -(S-
 8 (CH₂)_n-S)-; and wherein n is 2, 3 or 4.

1 16. A compound having the structure:

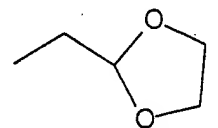


wherein R is hydrogen, a linear or branched alkyl, alkoxyalkyl, substituted or unsubstituted aryloxyalkyl, linear or branched acyl, substituted or unsubstituted aroyl or benzoyl; wherein X is a halogen; wherein R' is H, linear or branched chain alkyl, alkyl carboxaldehyde, alkyl carboxaldehyde linear or cyclic acetal; wherein R'' is H, linear or branched chain alkyl, phenyl, 2-methyl-1,3-thiazolyl, 2-furanyl, 3-furanyl, 4-furanyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, imidazolyl, 2-methyl-1,3-oxazolyl, 3-indolyl or 6-indolyl; and wherein Y is H or linear or branched chain alkyl.

17. A compound having the structure



wherein R is hydrogen, methyl, ethyl, n-propyl, n-hexyl, CO₂Et,



CH₂OH; or (CH₂)₃-OH; wherein R' and R'' are independently hydrogen, a linear or branched alkyl, substituted or unsubstituted aryl or benzyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, a linear or branched acyl, substituted or unsubstituted aroyl or benzoyl; and wherein Z is hydrogen, or linear or branched chain alkyl.

18. A method of preparing a Z-haloalkene ester having the structure:

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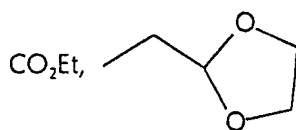


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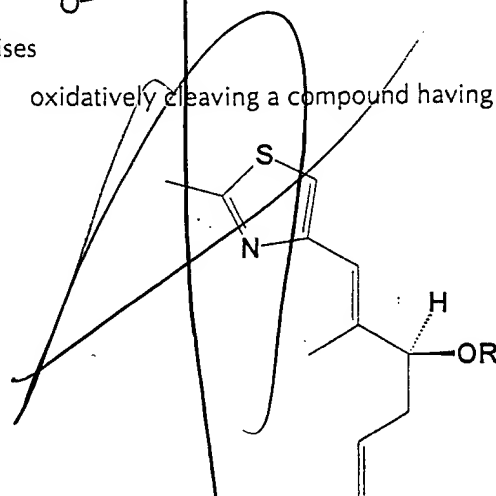
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under suitable conditions to form an aldehyde intermediate; and

(b) condensing the aldehyde intermediate with a halomethylene transfer agent under suitable conditions to form the Z-haloalkene ester.

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19. The method of claim 18 wherein X is iodine.

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20. The method of claim 18 wherein the halomethylene transfer agent is $\text{Ph}_3\text{P}=\text{CR}'\text{I}$ or $(\text{Ph}_3\text{P}^+\text{CHR}'\text{I})\text{I}^-$.

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21. A method of preparing an optically pure compound having the structure:

wherein R is hydrogen, a linear or branched alkyl, alkoxyalkyl, substituted or unsubstituted aryloxyalkyl, linear or branched acyl, substituted or unsubstituted aroyl or benzoyl, which comprises:

(a) condensing an allylic organometallic reagent with an unsaturated aldehyde having the structure:

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under suitable conditions to form an alcohol, and, optionally concurrently therewith, optically resolving the alcohol to form an optically pure alcohol having the structure:

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[illegible]

(b) alkylating or acylating the optically pure alcohol formed in step (a) under suitable conditions to form the optically pure compound.

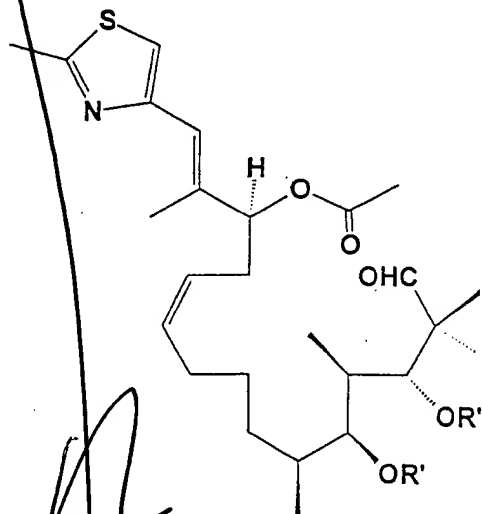
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1 22. The method of claim 21 wherein the allylic organometallic reagent is an
2 allyl(trialkyl)stannane.

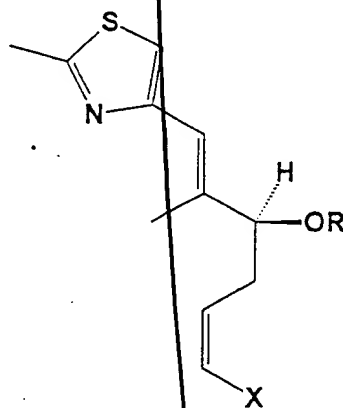
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OR'OR''CH(OR''')2

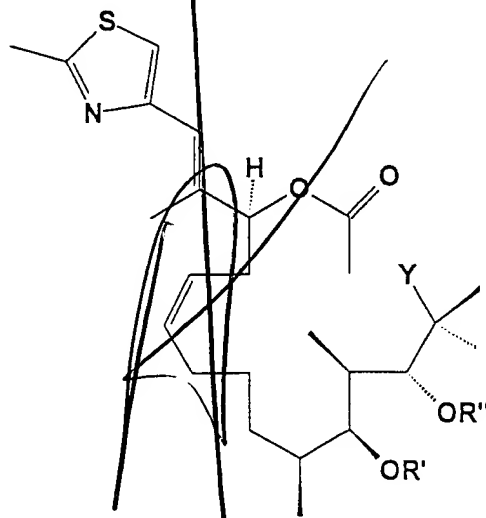
wherein $(OR''')_2$ is $(OR_0)_2$, $(SR_0)_2$, $-(O-(CH_2)_n-O)-$, $-(O-(CH_2)_n-S)-$ or $-(S-(CH_2)_n-S)-$ where R_0 is a linear or branched alkyl, substituted or unsubstituted aryl or benzyl; and wherein n is 2, 3 or 4, under suitable conditions to form a cross-coupled compound having the structure:

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wherein Y is $\text{CH}(\text{OR}^*)_2$ where R^* is a linear or branched alkyl, alkoxyalkyl, substituted or unsubstituted aryloxyalkyl; and

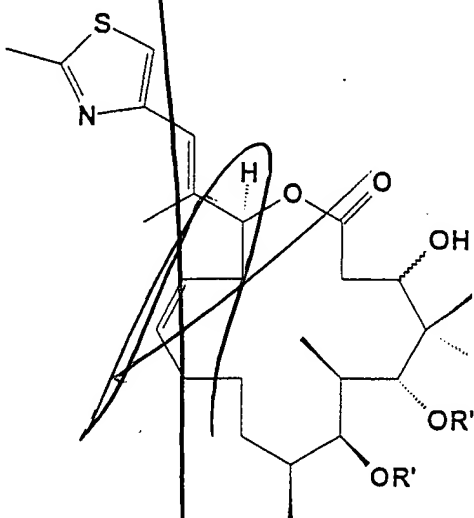
(b) deprotecting the cross-coupled compound formed in step (a) under suitable conditions to form the open-chain compound.

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26. A method of preparing an epothilone having the structure:

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(a) deprotecting a cyclized compound having the structure:



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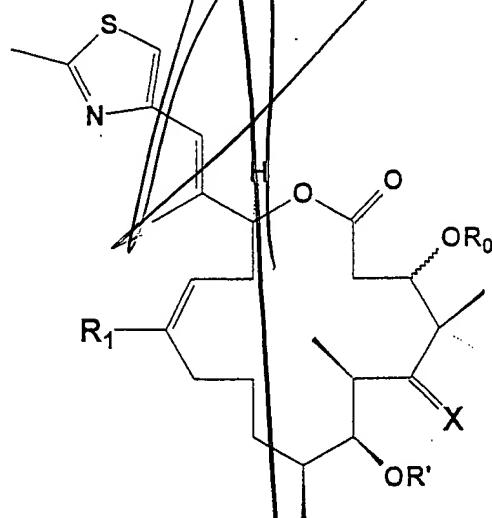
wherein R' and R'' are independently hydrogen, a linear or branched alkyl, substituted or unsubstituted aryl or benzyl, trialkylsilyl, dialkylarylsilyl, alkyl diarylsilyl, a linear or branched acyl, substituted or unsubstituted aroyl or benzoyl, under suitable conditions to form a deprotected cyclized compound and oxidizing the deprotected cyclized compound under suitable conditions to form a desoxyepothilone having the structure:

The diagram shows a chemical structure of a complex molecule, likely a nucleoside derivative. It features a thiazole ring (a five-membered ring with one sulfur atom 'S' and one nitrogen atom 'N') attached to a sugar moiety. The sugar moiety is a six-membered ring with several hydroxyl groups ('OH') and a carboxylic acid group ('COOH'). The structure is drawn with a vertical line representing the sugar backbone, and various substituents are shown branching off. The overall structure is complex and detailed, with many atoms and bonds explicitly drawn.

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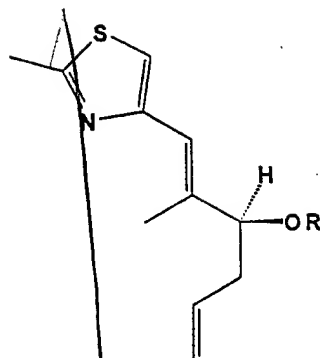
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(a) coupling a compound having the structure:

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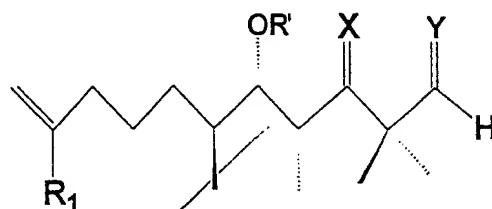


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wherein R is an acetyl, with an aldehyde having the structure:



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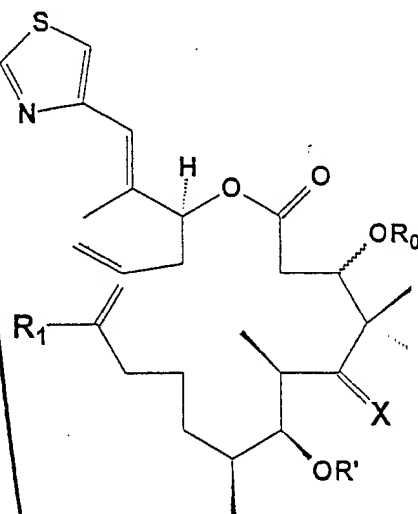
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wherein Y is oxygen, under suitable conditions to form an aldol intermediate and optionally protecting the aldol intermediate under suitable conditions to form an acyclic epothilone precursor having the structure:



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(b) subjecting the acyclic epothilone precursor to conditions leading to intramolecular olefin metathesis to form the epothilone precursor.

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28. The method of claim 27 wherein the conditions leading to intramolecular olefin metathesis require the presence of an organometallic catalyst.

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29. The method of claim 27 wherein the catalyst is a Ru or Mo complex.

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30. A pharmaceutical composition for treating cancer comprising a compound of claim 1,

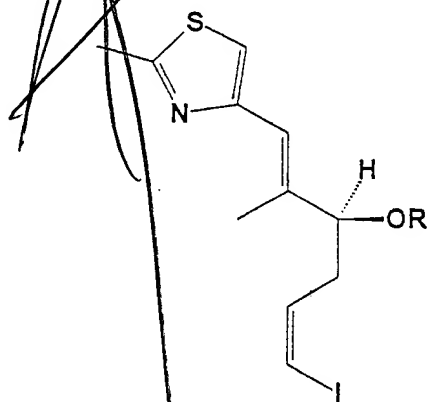
7, [REDACTED] and a pharmaceutically suitable carrier

31. A method of treating cancer in a subject suffering therefrom comprising administering to the subject a therapeutically effective amount of a compound of claim 1, 3, 5, 7 or 8 and a pharmaceutically suitable carrier.

32. The method of claim 31 wherein the cancer is a solid tumor.

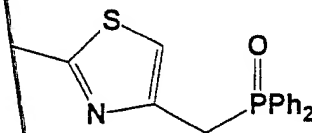
33. The method of claim 31 wherein the cancer is breast cancer.

34. A method of preparing a Z-iodoalkene ester having the structure:

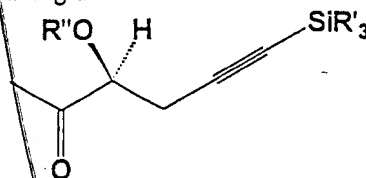


wherein R is hydrogen, a linear or branched alkyl, alkoxyalkyl, substituted or unsubstituted aryloxyalkyl, linear or branched acyl, substituted or unsubstituted aroyl or benzoyl, which comprises

(a) coupling a compound having the structure:

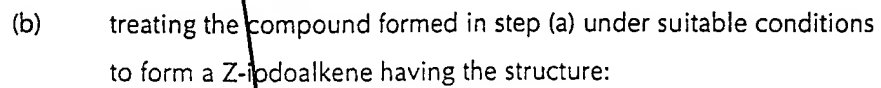


with a methyl ketone having the structure:



wherein R' and R'' are independently a linear or branched alkyl,

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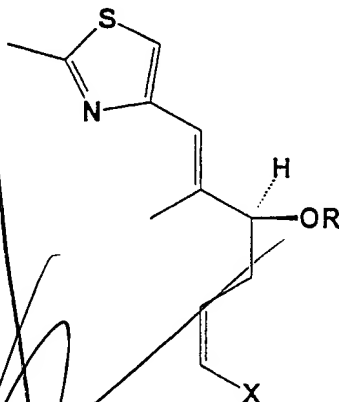
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35. A method of preparing an open-chain aldehyde having the structure:

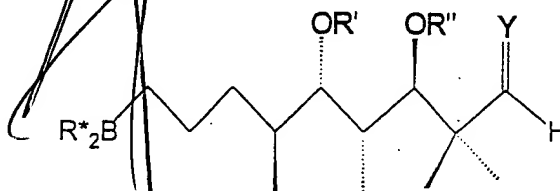


wherein R is a linear or branched alkyl, alkoxyalkyl, substituted or unsubstituted

(a) cross-coupling a haloolefin having the structure:



wherein X is a halogen, with a terminal hydroborane having the structure:



wherein R^+B is a linear, branched or cyclic alkyl or substituted or unsubstituted aryl or benzyl boranyl moiety; wherein Y is $(OR_0)_2$, $(SR_0)_2$, $-(O-(CH_2)_n-O)-$, $-(O-(CH_2)_n-S)-$ or $-(S-(CH_2)_n-S)-$ where R_0 is a linear or branched alkyl, substituted or unsubstituted aryl or benzyl; and wherein n is 2, 3 or 4, under suitable conditions to form a cross-coupled compound having the structure:

and

(b) deprotecting the cross-coupled compound formed in step (a) under suitable conditions to form the open-chain aldehyde.

36. The method of claim 35 wherein R is acetyl; R' is TBS; R'' is TPS; R*₂B is derived from 9-BBN; and Y is (OMe)₂.

37. A method of preparing a protected apothilone having the structure:

wherein R' and R'' are independently hydrogen, a linear or branched alkyl, substituted or unsubstituted aryl or benzyl, trialkylsilyl, dialkyl-arylsilyl, alkyldiarylsilyl, a linear or branched acyl, substituted or unsubstituted aroyl or benzoyl, which comprises:

(a) monoprotecting a cyclic diol having the structure:

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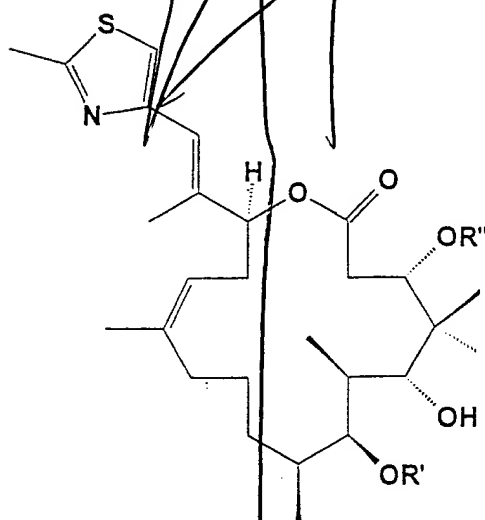
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under suitable conditions to form a cyclic alcohol having the structure:



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and

(b) oxidizing the cyclic alcohol formed in step (a) under suitable conditions to form the protected epothilone.

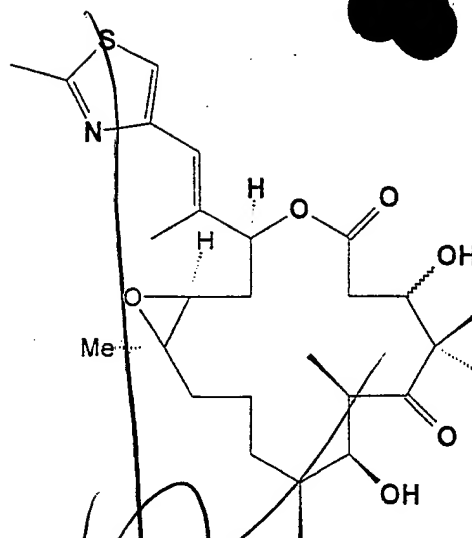
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38. The method of claim 37 wherein R' and R'' are TBS.

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39. A method of preparing an epothilone having the structure:

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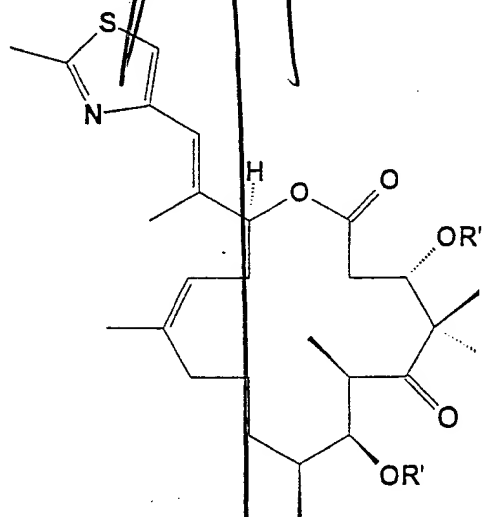
which comprises:

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(a) deprotecting a protected cyclic ketone having the structure:

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wherein R' and R'' are independently hydrogen, a linear or branched alkyl, substituted or unsubstituted aryl or benzyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, a linear or branched acyl, substituted or unsubstituted aroyl or benzoyl, under suitable conditions to form a desoxyepothilone having the structure:

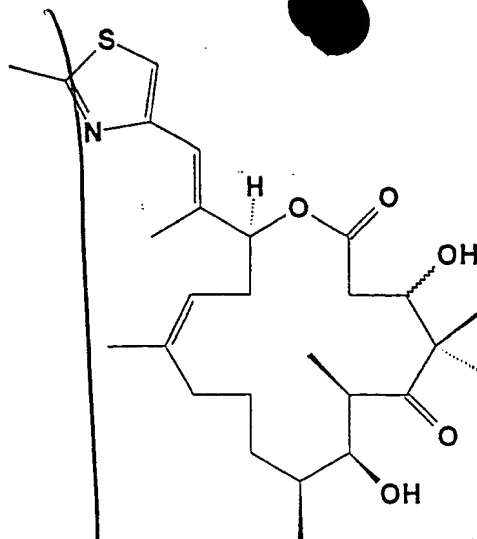
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(b) epoxidizing the desoxyepothilone formed in step (a) under suitable conditions to form the epothilone.

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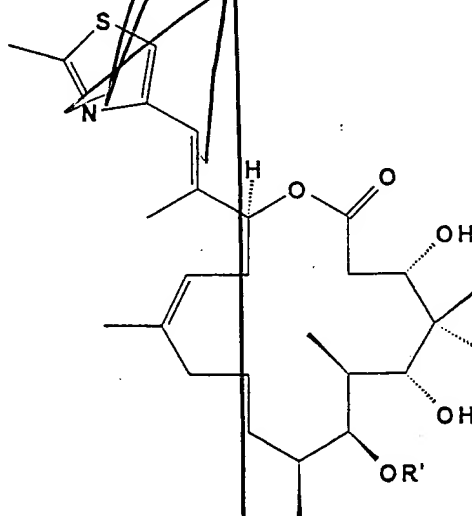
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40. The method of claim 39 wherein R' and R'' are TBS.

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41. A method of preparing a cyclic diol having the structure:

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wherein R' is a hydrogen, a linear or branched alkyl, substituted or unsubstituted aryl or benzyl, trialkylsilyl, dialkylarylsilyl, alkyl diarylsilyl, a linear or branched acyl, substituted or unsubstituted aroyl or benzoyl, which comprises:

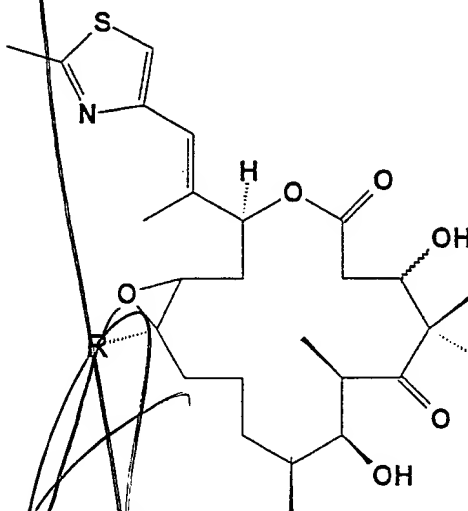
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(a) cyclizing an open-chain aldehyde having the structure:

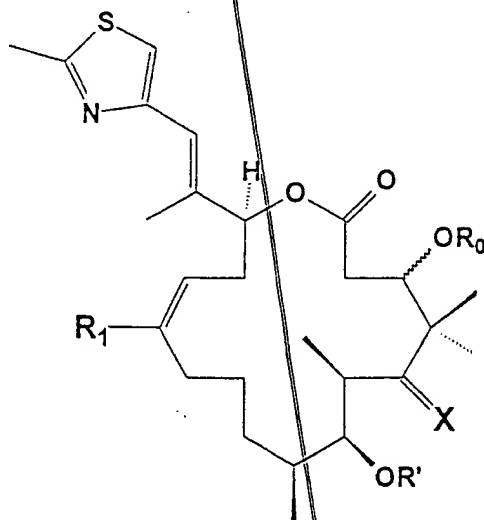
1 42. The method of claim 41 wherein R' is TBS and R'' is TPS.

1 43. A purified compound having the structure:
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3
4



5 wherein R is hydrogen, methyl, ethyl, propyl, hexyl, hydroxymethyl or
6 hydroxypropyl; wherein X is O; and wherein R₀, R' and R'' are independently
7 hydrogen or acetyl.
8

1 44. A purified compound having the structure:
2



3 wherein R₁ is hydrogen, methyl, ethyl, propyl, hexyl, hydroxymethyl or
4 hydroxypropyl; wherein X is O; and wherein R₀, R' and R'' are independently
5 hydrogen or acetyl.
6

1 45. A composition comprising an amount of the compound of claim 1, 2, 3, 4, 5, 6, 7, 8,
2 43 or 44 effective to inhibit the growth of multidrug resistant cells and a

said mixture comprising an α - and a β -alcohol component;
optionally isolating and oxidizing the α -alcohol formed in step (a) under suitable conditions to form a ketone and thereafter reducing the ketone under suitable conditions to form an enantiomeric mixture of the protected cyclic alcohol comprising substantially the β -alcohol; and
treating the protected cyclic alcohol formed in step (a) or (b) with a deprotecting agent under suitable conditions to form the cyclic diol.

3 pharmaceutically acceptable carrier.

1 46. The composition of claim 45, further comprising an amount of a cytotoxic agent.

1 47. The composition of claim 46, wherein the cytotoxic agent is an anticancer agent.

1 48. The composition of claim 47, wherein the anticancer agent is adriamycin.

1 49. The composition of claim 47, wherein the anticancer agent is vinblastin.

1 50. The composition of claim 47, wherein the anticancer agent is paclitaxel.

1 51. The composition of claim 45, wherein the effective amount of the compound is
2 between about 0.01 mg/kg to about 25 mg/kg of body weight.

1 52. A method of inhibiting the growth of multidrug resistant cells comprising contacting
2 the multidrug resistant cells with an amount of the compound of claim 1, 2, 3, 4, 5,
3 6, 7, 8, 43 or 44 effective to inhibit the growth of multidrug resistant cells in
4 combination with a pharmaceutically acceptable carrier.

1 53. The method of claim 52, further comprising administering an amount of a cytotoxic
2 agent.

1 54. The method of claim 53, wherein the cytotoxic agent is an anticancer agent.

1 55. The method of claim 54, wherein the anticancer agent is adriamycin.

1 56. The method of claim 55, wherein the anticancer agent is vinblastin.

1 57. The method of claim 55, wherein the anticancer agent is paclitaxel.

1 58. The method of claim 55, wherein the effective amount of the compound is between
2 about 0.01 mg/kg to about 25 mg/kg of body weight.

ACKIAZ